

REVIEW PAPER

A systematic review: non-pharmacological interventions in treating pain in patients with advanced cancer

Minna Hökkä, Pirjo Kaakinen & Tarja Pölkki

Accepted for publication 3 March 2014

Correspondence to M. Hökkä:
e-mail: minnahokka@hotmail.com

Minna Hökkä MNSc RN
Nursing Teacher
Institution of Health Sciences, University of
Oulu, Finland

Pirjo Kaakinen RN
Doctoral Student
Institution of Health Sciences, University of
Oulu, University Hospital of Oulu, Finland

Tarja Pölkki PhD RN
Adjunct Professor
Institution of Health Sciences, University of
Oulu, Finland

HÖKKÄ M., KAAKINEN P. & PÖLKKI T. (2014) A systematic review: non-pharmacological interventions in treating pain in patients with advanced cancer. *Journal of Advanced Nursing* 00(0), 000–000. doi: 10.1111/jan.12424

Abstract

Aims. To assess and synthesize the evidence of the effects and safety of non-pharmacological interventions in treating pain in patients with advanced cancer.

Background. Pain is a common symptom experienced by patients with advanced cancer; the treatment of such pain is often suboptimal. To manage it, non-pharmacological interventions are recommended after pharmacological treatments have been re-evaluated and modified. However, there remains a lack of knowledge about the effects and safety of such interventions.

Design. A systematic review was conducted based on the procedure of the Centre of Reviews and Dissemination.

Data Sources. Research papers published between 2000–2013 were identified from the following databases: CINAHL, MEDIC, MEDLINE (Ovid) and PsycINFO. The references in the selected studies were searched manually.

Review Methods. The studies selected were reviewed for quality, using Cochrane Effective Practice and Organisation of Care Review Group risk of bias assessment criteria.

Results. There was limited evidence that some of the non-pharmacological interventions were promising with respect to reducing cancer pain. Relatively, few adverse events were reported as a result of using such interventions.

Conclusion. It was not possible to draw conclusions about the effects and safety of the non-pharmacological interventions in reducing cancer pain. Some interventions showed promising short-term effects, but there is a need for more rigorous trials. Qualitative studies are required to collect information about patients' perceptions. There are several research gaps: we found no studies about music, spiritual care, hypnosis, active coping training, cold or ultrasonic stimulation.

Keywords: adult care, cancer, complementary therapy, holistic care, literature review, non-pharmacological intervention, nursing, pain, palliative care

Why is this research or review needed?

- Globally, cancer is a leading cause of death and pain is one of the most common symptoms in patients with advanced cancer.
- Treatment of cancer pain is an important concern in health care, especially when its treatment has been shown to be suboptimal.
- Some studies have focused on non-pharmacological interventions in managing advanced cancer pain; however, there is a lack of systematic reviews regarding this research topic.

What are the key findings?

- The non-pharmacological interventions explored in the studies examined showed marginal beneficial effects in reducing cancer pain in patients with advanced cancer.
- There was a lack of statistical and clinical significance between groups and there were limitations associated with the studies included in the review.
- The non-pharmacological interventions were quite well tolerated; however, the lack of systematic data and reporting of the safety of the interventions meant that no definitive conclusions could be drawn.

How should the findings be used to influence practice and research?

- There is a need for more rigorous trials of the effects and safety of non-pharmacological interventions such as music, hypnosis, active coping training and cold to manage cancer pain.
- There is also a gap relating to knowledge about implementing non-pharmacological interventions in outpatient settings for patients with advanced cancer.
- Healthcare providers should be aware of the different non-pharmacological interventions, but how these interventions should be used remains unclear until further evidence is available.

Introduction

The World Health Organization (WHO) estimates that 7.6 million people died from cancer in 2008 and globally cancer is a leading cause of death (WHO 2005, 2013). Patients with advanced or metastatic cancer have a life-threatening illness, requiring special care. The WHO definition of palliative care is that it is 'an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other

problems, physical, psychosocial and spiritual' (WHO 2013).

Pain is one of the most common symptoms and a substantial burden for patients with cancer (Goudas *et al.* 2005). Approximately 64–75% of patients with advanced or terminal cancer experience pain (van den Beuken-van Everdingen *et al.* 2007a,b). Treatment of cancer pain is an important concern in health care, especially when its treatment has been shown to be suboptimal (van den Beuken-van Everdingen *et al.* 2007a,b, Breivik *et al.* 2009).

The International Association for the Study of Pain (IASP) defines pain as 'an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage' (IASP 2012). Cancer pain is often categorized by determining whether the symptoms are neuropathic or nociceptive (Paice & Ferrell 2011). Neuropathic pain is caused by a lesion or dysfunction in the nervous system, which is often complex to treat. Nociceptive pain occurs when the nociceptors activate because of an actual or threatened damage to non-neural tissue (Urch & Dickenson 2008, IASP 2012). Cancer pain is often a combination of different pain mechanisms (Laird *et al.* 2008, Urch & Dickenson 2008).

The biopsychosocial and integrated psychosocial–spiritual models for cancer pain management maintain that, in addition to biological factors, pain is also influenced by psychological factors (e.g. mood factors), social factors (e.g. responses of partners and caregivers) and spiritual factors (e.g. existential distress) (Otis-Green *et al.* 2002, Sutton *et al.* 2002). Management of general distress, symptoms such as fear, anxiety or depression, will reduce pain through a direct influence on pain pathways (Laird *et al.* 2008).

Melzack and Wall (1965) introduced the gate control theory of pain. The theory states that, in addition to pain pathways, there are additional pathways that influence the signal sent from the spinal cord to the brain. These additional pathways can act to open or close a gate in the spinal cord and this determines the strength of the signal leaving the spinal cord. The gate control system consists of small cells extending the length of the spinal cord. The theory suggests that psychological factors influence pain response and perception by acting on the gate control system. (Melzack & Wall 1965). This theory has also been employed to explain the benefits of non-pharmacological interventions such as TENS, the application of cold or heat and cognitive behavioural approaches in pain alleviation (Hansson & Lundberg 1999, Lehmann & de Lateur 1999, Turk & Okifuji 1999).

Cancer pain is a multidimensional phenomenon. Thus, even if pharmacological analgesics are the cornerstone of

managing it, the American National Comprehensive Cancer Network (ANCCN) also recommends the use of non-pharmacological interventions (Table 1) if pain scores remain at 4 or above on a 10-point scale after the pharmacological treatment has been re-evaluated and modified (Swarm *et al.* 2010). Non-pharmacological interventions, in this case, are used as complementary therapies. When such interventions are used in conjunction with conventional therapies, the approach is known as 'integrative medicine' (Cohen 2004, Deng & Cassileth 2005).

Globally, cancer is a leading cause of death and pain is one of the most common symptoms; even so, its treatment has been shown to be suboptimal (WHO 2005, 2013, van den Beuken-van Everdingen *et al.* 2007a,b, Breivik *et al.* 2009). Complementary therapies are widely used among patients with cancer (Deng & Cassileth 2005). However, there is a lack of knowledge of the benefits and safety of non-pharmacological interventions when managing pain in patients with advanced cancer. We therefore felt that it was important to undertake a systematic review of the patient to provide information for the healthcare professionals and to identify gaps in the knowledge that require further research.

The review

Aim

The aim of the systematic review was to assess and synthesize the current available clinical evidence concerning the use of non-pharmacological therapies in treating cancer pain.

The research questions were as follows:

- Are non-pharmacological therapies effective in reducing cancer pain for patients with advanced cancer?

Table 1 Non-Pharmacological interventions (Bardia *et al.* 2006, Wilkinson *et al.* 2008b, Swarm *et al.* 2010).

Physical modalities	Cognitive modalities
Bed, bath and walking supports"	Imagery/Hypnosis
Position instruction, Physical therapy	Distraction training
Energy conservation, pacing of activities	Relaxation training
Massage	Active coping training
Heat and/or ice	Cognitive behavioural training
Transcutaneous electrical nerve stimulation (TENS)	Spiritual care
Acupuncture or acupressure	Creating outlets, such as music
Ultrasonic stimulation	
Reflexology	

- Are non-pharmacological therapies safe for patients with advanced cancer?

Design

A systematic review was conducted following the procedure for conducting such reviews of health interventions outlined by the Centre for Reviews and Dissemination (2008).

Search methods

With the help of an information specialist, a search strategy was devised to identify studies that met our inclusion criteria (Table 2) (Whittemore 2005). To identify the best relevant terms for the final searches, preliminary trials were undertaken.

Four databases were systematically searched to identify relevant studies: CINAHL, MEDIC (the Finnish database of Medicine and Health Sciences), MEDLINE (Ovid) and PsycINFO. The search years were limited to the period from 2000–30 January 2013 to ensure that the studies included were up-to-date. The following key terms were used: 'palliative care or hospice care or terminally ill' and 'complementary therapies/methods or non-pharmacological' and 'neoplasms or cancer' and 'pain or pain management'. The key MESH terms were exploded if possible in the databases. The terms were modified as necessary for each database. Manual searches were also undertaken of the references in the selected studies and also in four publications (*Journal of Advanced Nursing*, *Journal of Hospice & Palliative Nursing*, *Hoitotiede*, *Tutkiva Hoitotyö*).

Table 2 Inclusion and exclusion criteria.

Inclusion	Exclusion
Written in English, Finnish or Swedish	Written in other languages
Paper's main focus on non-pharmacological interventions in treating cancer pain	Focusing on interventions other than non-pharmacological ones
Palliative, hospice or end-of-life care patients with advanced cancer.	Not focusing on palliative care or advanced patients with cancer or patients' stage of cancer not described.
Papers focusing on adults (over 18 years)	Papers focusing on children or adolescents under 18 years
Date limit 2000–early 2013	Not a peer-reviewed empirical research article
Peer-reviewed empirical research articles	Full-text not available
Full-text available	

Inclusion and exclusion criteria

We only included studies published in English, Swedish or Finnish in the review. There were no research methodology limitations in this phase of the search strategy. The other inclusion criteria were in line with the aim of the review. The participants: adult patients with advanced cancer. Intervention: all non-pharmacological interventions defined by Bardia *et al.* (2006) and Swarm *et al.* (2010) (Table 1). Outcome: Reduction in pain in terms of perceived pain control and experience, pain intensity and pain interference. We included studies that used appropriate and valid processes or measures to evaluate the evidence of the efficacy and safety of non-pharmacological interventions in pain reduction for patients with advanced cancer. We excluded studies where the participants' state of the cancer was not described and those that included patients with cancer not at an advanced stage. We also excluded literature reviews. (Table 2).

Search outcome

The searching process was carried out during the period November 2012–January 2013. The searches were made

systematically, and as Moher *et al.* (2009) recommend, all details of the study identification and selection process are shown in a PRISMA flow chart (Figure 1). The database searches yielded 460 relevant titles. The manual search produced two additional titles. The duplicates were identified (by MH) resulting in a final tally of 444 titles. As a result of reading the titles and abstracts (this was undertaken by MH and TP), 376 studies were rejected.

Articles were rejected because they did not meet the inclusion criteria, i.e. their main focus was not on non-pharmacological intervention or advanced patients with cancer. There were also papers that did not meet the language criteria or where the patients were children or adolescents under 18 years. A total of 68 full texts were retrieved and read (by MH and TP), of which 10 met the inclusion criteria and were included in the final selection. If there was uncertainty or disagreement about inclusion, the reviewers re-evaluated the article together and came to an agreement about whether or not to include it. The references in these 10 articles were also searched and, as a result, one additional article was found that met the inclusion criteria. More detailed information about excluded studies is included in Table S1.

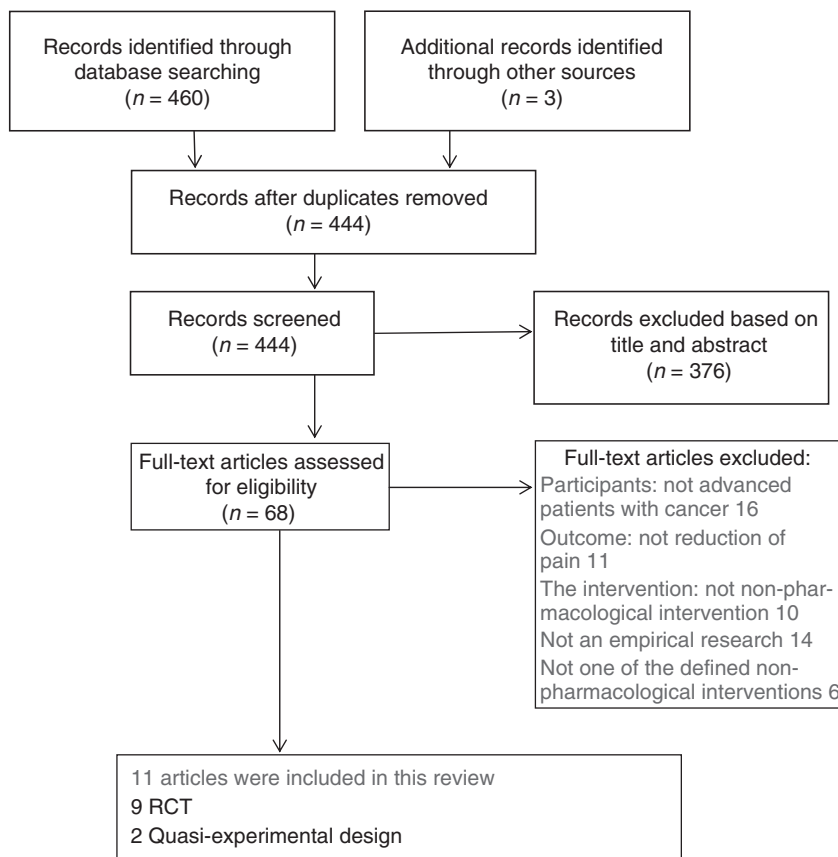


Figure 1 PRISMA flow chart.

Quality appraisal

To assess the quality of the studies selected, we used the risk of bias assessment tool recommended by the Cochrane Collaboration to address the following six domains: sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting and other sources of bias (Higgins & Green 2009).

Before the assessment, the authors (MH and PK) discussed and read through the documentation describing the tool to ensure that they both had a similar understanding of the assessed domains. The quality of the different studies was independently evaluated by the authors, after which the authors compared their evaluations.

Data abstraction

Data extraction was conducted using a form that was developed for this review and that was piloted on a sample of 10 articles (Jones & Evans 2000, Centre for Reviews & Dissemination 2008, Joanna Briggs Institute 2008). Data were extracted from each study about the intervention, outcome measures and methodology (Table 3), as well as the setting and sample (age, sex, stage of cancer, site of cancer) (Table 4).

Synthesis

The search produced nine RCT and two quasi-experimental studies that met the inclusion criteria and were included in this review. The results of the relevant studies were summarized using a narrative approach, because the studies were heterogeneous, differing in their purpose, interventions and outcome measurement tools (Lloyd Jones 2004, Centre for Reviews & Dissemination 2008, Whiting 2009, Polit & Beck 2011).

Results

Methodological quality

Randomized controlled trials

The randomized sequence generation process was described in six of the studies (Kutner *et al.* 2008, Bennett *et al.* 2010, Jane *et al.* 2011, Lim *et al.* 2011, Lopez-Sendin *et al.* 2012, Wyatt *et al.* 2012). In three of the studies, it remained unclear whether there had been adequate randomization; there were statements that randomization was undertaken, but the method and process were not described (Soden *et al.* 2004, Tsai *et al.* 2007, Yamamoto & Nagata 2011). Whether the allocation sequence was

concealed was not clear in four of the RCTs because concealment was not described (Tsai *et al.* 2007, Bennett *et al.* 2010, Yamamoto & Nagata 2011, Lopez-Sendin *et al.* 2012). In the other five RCTs, concealment was undertaken and was described adequately (Soden *et al.* 2004, Kutner *et al.* 2008, Jane *et al.* 2011, Lim *et al.* 2011, Wyatt *et al.* 2012).

In the RCTs, blinding was adequately described in one study (Soden *et al.* 2004). In four of the RCTs, the blinding process remained unclear because it was not described and in one study, the blinding was not achieved (Tsai *et al.* 2007, Bennett *et al.* 2010, Lim *et al.* 2011, Yamamoto & Nagata 2011, Lopez-Sendin *et al.* 2012). In the other three RCTs, the lack of blinding of patients, data collectors or therapists may have increased the risk of bias (Kutner *et al.* 2008, Jane *et al.* 2011, Wyatt *et al.* 2012).

In general, withdrawal was described in the RCTs. In two studies, withdrawal of participants was described and the reasons were given; in these studies, the authors also described how the missing outcomes were analysed and tested and how the missing data could have affected the outcomes (Kutner *et al.* 2008, Wyatt *et al.* 2012). In one RCT, withdrawals were described, but the reasons were not presented (Lim *et al.* 2011). In one of the studies, the high withdrawal rate could have biased the results (Lopez-Sendin *et al.* 2012). In the other five studies, withdrawal was described, but it remained unclear whether it influenced the main outcomes (Soden *et al.* 2004, Tsai *et al.* 2007, Bennett *et al.* 2010, Jane *et al.* 2011, Yamamoto & Nagata 2011).

The main outcomes were described in six of the studies. In three, there were difficulties in finding statistical evidence for the effects between groups (Soden *et al.* 2004, Lim *et al.* 2011, Yamamoto & Nagata 2011). Within group, effects were highlighted. In one study, there was a risk of bias because there were baseline differences between groups and in one RCT, the lack of a 'usual care' control group may have increased the risk of bias (Tsai *et al.* 2007, Kutner *et al.* 2008). More detailed information about the quality of included RCTs is included in Table S2.

Quasi-experimental studies

In the quasi-experimental studies, the inclusion criteria for the participants were well described. (Jane *et al.* 2009, Kwekkeboom *et al.* 2010). The studies used convenience samples and the sampling was well described. One of the studies did not use blinding (Jane *et al.* 2009). In the other study, the risk of bias was reduced because the data collector was blinded and did not provide the intervention (Kwekkeboom *et al.* 2010).

Table 3 Data extraction.

Author	Study aim	Method/Design and sample	Pain measurement tools	Non-pharmacological intervention	Findings: Effects on pain	Findings: Adverse events
Bennett <i>et al.</i> (2010) UK	To investigate the feasibility of running a large-scale phase III trial to investigate the efficacy of active TENS in the control of cancer pain.	Randomized crossover trial of TENS or placebo. Baseline assessment was undertaken. Pain was assessed during TENS sessions (lasting 30 and 60 minutes). <i>n</i> analysed 19	Numerical Rating Scale (NRS) Short-form McGill Pain Questionnaire (SF-MPQ)	One-armed transcutaneous electrical nerve stimulation (TENS) session and one placebo TENS session. Median interval between applications 3 days.	TENS has the potential to decrease pain during movement (difference between groups 14.2, 95% CI = -3.34, 31.76) more than pain during rest (difference between groups -1.32, 95% CI = -3.42 to 0.79).	9 patients experienced adverse events. Distribution of adverse events was similar following active or placebo TENS application. 3 of the events were possibly related to the TENS. 1 event was related to placebo TENS. No participants reported any adverse events
Jane <i>et al.</i> (2009) Taiwan	To describe the feasibility of full-body massage and to examine the effects of massage on present pain intensity and other symptoms	Quasi-experimental one-group, pre-test-posttest design with repeated measures. <i>n</i> analysed 30	Present Pain Intensity (PPI) with a vertical form of the visual analogue scale (VAS) (PPI-VAS)	38–50 minutes of massage therapy, which followed a standardized protocol.	Effects: immediate ($P < 0.001$) short-term ($P < 0.001$) intermediate ($P = 0.000$) long-term benefits ($P < 0.001$)	
Jane <i>et al.</i> (2011) Taiwan	To compare the efficacy of massage therapy (MT) with a social attention (SA) control condition on pain intensity	RCT of MT vs. SA. Assessments were undertaken pre- and posttest. <i>n</i> analysed 72.	Present Pain Intensity (PPI) with a vertical form of the visual analogue scale (VAS) (PPI-VAS)	45 minutes of MT, which followed a standardized protocol. 5-day research protocol, which included three sessions of MT or SA	Significant group differences at each time point; $P < 0.001$ (T1); $P < 0.001$ (T2); $P = 0.001$ (T3). Time effect of PPI-VAS between groups over time $P < 0.000$, Reduction in PPI-VAS converged over time.	Adverse events were not described in the article
Kurner <i>et al.</i> (2008) United States	To evaluate the efficacy of massage for decreasing pain and other symptoms	RCT of massage therapy or simple-touch therapy. Baseline assessment and sustained assessment was undertaken three times.	Memorial Pain Assessment Card and Brief Pain Inventory (BPI)	Six 30-minute massage or simple-touch sessions over 2 weeks.	Massage had immediately beneficial effects on pain (-1.87 points (95% CI -2.07 to 1.67)) massage therapy did not	Adverse events were infrequent and similar in both groups and did not

Table 3 (Continued).

Author	Study aim	Method/Design and sample	Pain measurement tools	Non-pharmacological intervention	Findings: Effects on pain	Findings: Adverse events
		Assessments were also undertaken immediately after each intervention. <i>n</i> analysed 380			was statistically superior to the control group (mean pain difference between study groups, -0.90 points (CI -1.19 to -0.61 points)) but not clinically significant. No sustained improvement in pain outcomes (BPI mean pain, 0.07 points (CI -0.23 to 0.37 points); BPI worst pain, -0.14 points (CI -0.59 to 0.31 points)).	seem to be related to treatments
Kwekkeboom <i>et al.</i> (2010) United States	To evaluate the feasibility of a patient-controlled cognitive behavioural intervention for pain and other symptoms.	One-group pre- and posttest design. Outcomes were assessed before and after using a cognitive behavioural strategy. <i>n</i> analysed 30	Brief Pain Inventory (BPI)	The intervention included recordings of 12 brief cognitive strategies provided on an MP3 player. Cognitive behavioural strategies included relaxation, distraction and imagery exercises in four categories. Two weeks intervention.	Immediate changes in symptom ratings from pre- to posttest treatment were significant $P < 0.01$.	Adverse events were not reported
Lim <i>et al.</i> (2011) Canada	To document changes in symptoms after acupuncture or nurse-led supportive care in patients with incurable cancer	RCT of acupuncture or nurse-led supportive care. The assessments were undertaken before and after each intervention. In addition, scores were obtained via weekly telephone interviews for 6 weeks following completion of each intervention. <i>n</i> analysed 18	Edmonton Symptom Assessment System (ESAS)	Weekly acupuncture for 4 weeks or weekly nurse-led supportive sessions, which included counselling and discussion.	Mean change in ESAS score after acupuncture -1.5. At 6 weeks, +0.5. No significant pain reduction compared with the social attention group.	Two minor adverse events/ side effects. No significant or unexpected side effects.

Table 3 (Continued).

Author	Study aim	Method/Design and sample	Pain measurement tools	Non-pharmacological intervention	Findings: Effects on pain	Findings: Adverse events
Lopez-Sendin <i>et al.</i> (2012) Spain	To determine the effects of therapy, including massage and exercise, on pain and mood in patients with advanced terminal cancer.	RCT of physiotherapy or simple hand contact. Assessments were conducted at baseline, at 1 week and at a 2-week follow-up. <i>n</i> analysed 24	Memorial Pain Assessment Card and Brief Pain Inventory (BPI)	Six sessions of 30–35 minutes duration over 2 weeks. The intervention consisted of different massage techniques and strain/counter strain techniques over the tender points. In addition, the intervention included passive mobilization exercises.	Group \times time interaction with greater improvements in physical therapy group for BPI worst pain ($P = 0.036$), BPI pain right now ($P = 0.027$) and BPI index ($P = 0.001$). No significant differences in BPI with respect to mean ($P = 0.127$) and least pain ($P = 0.027$)	Adverse events were not reported.
Soden <i>et al.</i> (2004) United Kingdom	The primary aim was to compare the longer term effects of a course of massage with or without an essential oil on pain scores. Secondary aims were to test the hypothesis that these therapies improve sleep quality, reduce anxiety and depression and improve overall quality of life	RCT of aromatherapy massage group or no intervention group. Pain and other symptoms were assessed before and after intervention and weekly during the intervention. <i>n</i> analysed 42	Visual Analogue Scale (VAS)	Standardized 30-minute back massage weekly for 4 weeks. The aromatherapy massage group had essential (lavender) oil applied and the other group normal massage oil.	No significant long-term benefits of aromatherapy or massage in terms of improving pain control. Significant effect in pain VAS score after the second treatment.	Adverse events were not reported.
Tsai <i>et al.</i> (2007) Taiwan	To examine the effect of EMG biofeedback-assisted relaxation on cancer-related pain.	RCT of EMG biofeedback-assisted relaxation or conventional care. Symptoms assessed before and after first and last EMG session. <i>n</i> analysed 24	Brief Pain Inventory (BPI)	Six EMG biofeedback-assisted relaxation sessions during a 4-week period.	The experimental group reported a statistically significant decrease in pain intensity from baseline, compared with the control group ($P < 0.001$)	Adverse events were not reported in the research.
Wyatt <i>et al.</i> (2012) United States	To evaluate the safety and efficacy of reflexology	RCT of reflexology or lay foot manipulation or conventional care. Outcomes were assessed at baseline interview, postintervention interview	Brief Pain Inventory (BPI) short form	30 minutes of stimulation to the nine essential breast cancer-specific reflexes while using reflexology-specific deep thumb-walking pressure.	No difference was found on breast cancer-specific HRQOL, depressive symptomatology state of anxiety, pain and nausea	No adverse events were reported on the standard forms used in the interventions

Table 3 (Continued).

Author	Study aim	Method/Design and sample	Pain measurement tools	Non-pharmacological intervention	Findings: Effects on pain	Findings: Adverse events
Yamamoto and Nagata (2011) Japan	To clarify the effects of a warm water-footbath on relaxation, pain and mood in patients with cancer.	RCT of WW-footbath or no WW-footbath. Pre-test and posttest assessment. Heart rate variable measurement during intervention. <i>n</i> analysed 9	Visual Analogue Scale (VAS)	The lay foot manipulation was designed to appear superficially similar to reflexology. Four weekly 30 minutes sessions The 30-minute WW-footbath procedure was given to the patients	The posttest pain VAS score significantly decreased in the experimental group ($P = 0.047$). No significant between-groups changes.	Adverse events were not reported in the research.

Participants and setting

The studies were undertaken in the USA ($n = 3$), the UK ($n = 2$), Taiwan ($n = 3$), Canada ($n = 1$), Japan ($n = 1$) and Spain ($n = 1$) and were dated between 2004–2012. Sample sizes ranged from 18 to 385 participants. The participants were adults aged 33–85 and they had a wide range of cancer diagnoses. The total number of participants in this current review was 1047, of these, 74% were female and 26% male. All participants in the studies had advanced, metastatic or incurable cancer; the papers reported on nine inpatient settings and two outpatient settings. The two non-pharmacological interventions that were tested in outpatient settings were reflexology (Wyatt *et al.* 2012) and cognitive behavioural interventions (Kwekkeboom *et al.* 2010). (Table 4).

Description of interventions

The physical modalities examined in the studies included were massage (Soden *et al.* 2004, Kutner *et al.* 2008, Jane *et al.* 2009, 2011), aromatherapy massage (Soden *et al.* 2004), physical therapy (Lopez-Sendin *et al.* 2012), transcutaneous electrical nerve stimulation (TENS) (Bennett *et al.* 2010), acupuncture (Lim *et al.* 2011) and wrapped warm footbath (Yamamoto & Nagata 2011). The cognitive modalities that were described consisted of cognitive behavioural strategies in the form of relaxation, distraction and imagery exercises (Tsai *et al.* 2007).

Massage was the intervention that was examined most frequently. Four of the papers considered massage (Soden *et al.* 2004, Kutner *et al.* 2008, Jane *et al.* 2009, 2011). Soden *et al.* (2004) explored massage with and without aromatherapy. The control exposures used in the trials were simple touch (Kutner *et al.* 2008) and social attention (Jane *et al.* 2011). Lopez-Sendin *et al.* (2012) explored physical therapy, which included massage, exercise or simple hand contact. Massage lasted, on average, 30–50 minutes. In three studies (Soden *et al.* 2004, Jane *et al.* 2009, 2011), the massage intervention followed a standardized protocol. The massage therapy providers were Registered Nurses (Jane *et al.* 2011), therapists (Soden *et al.* 2004, Kutner *et al.* 2008) and physiotherapists (Lopez-Sendin *et al.* 2012).

TENS was used as a non-pharmacological intervention for cancer bone pain in the study by Bennett *et al.* (2010). The participants had TENS applied to the site of the bone pain. The intervention lasted for a week and the participants received the TENS treatment, delivered by a medical researcher, twice. Acupuncture was the non-pharmacological intervention used in the study by Lim *et al.* (2011). The participants received weekly acupuncture for 4 weeks. The

Table 4 Participants characteristics.

Author	Cancer sites	Gender	Age	Cancer stage	Other socio-demographic information
Bennett <i>et al.</i> (2010)	Prostate, breast, lung, thyroid, renal, other	Female 6 male 18 <i>n</i> = 24	Median 69 years range 40–83 years	Metastatic cancer	Setting: specialist palliative care service
Jane <i>et al.</i> (2009)	Lung, breast, head and neck, GI cancer, genitourinary cancer	Female 19 (63%) male 11 (37%) <i>n</i> = 30	Mean years 52 range 33–75 years	Metastatic cancer	Inpatient oncology units
Jane <i>et al.</i> (2011)	Lung, breast, head and neck, GI cancer, genitourinary cancer, other	Female 42 (58%) male 30 (42%) <i>n</i> = 72	49.9±10.6 years	Metastatic cancer	Setting: inpatient oncology units
Kurmer <i>et al.</i> (2008)	Lung, breast, pancreatic, colorectal, prostate	Therapy group female 120 (64%), male 68 Control group female 112 (58%), male 80 <i>n</i> = 380	Therapy group mean 65.2 years Control group mean 64.2 years range not reported	Metastatic cancer advanced cancer	90% of the patients were in a hospice.
Kwekkeboom <i>et al.</i> (2010)	Gynaecological, lung, colorectal, prostate	Female 24 male 6 <i>n</i> = 30	Range 36–79 years mean 56.27 years	Advanced (recurrent or metastatic) cancer	Outpatient oncology clinics at a comprehensive cancer centre
Lim <i>et al.</i> (2011)	Breast, rectum, endometrium, cervix, oropharynx, bladder, leukaemia, kidney, myeloma, lung, caecum, oesophagus	Female 15 male 3 <i>n</i> = 18	Acupuncture group mean 55 years, range 31–72 years Nurse-led supportive care mean 64.9 years, range 53–81 years	Advanced incurable cancer	Outpatients, the intervention was conducted in a Pain and Symptom Clinic
Lopez-Sendin <i>et al.</i> (2012)	Lung, melanoma, sarcoma, prostate, Colon, pancreas and breast	Therapy group (male/female) 8/4 Control group (male/female) 10/2 Female 32 (76%) male 10 (24%)	Control group years 58±8 Therapy group years 55±21	Advanced terminal cancer	The patients were in a specialist oncology university hospital
Soden <i>et al.</i> (2004)	Breast, lung, gastrointestinal, head and neck, prostate, other	Female 32 (76%) male 10 (24%)	Mean 73 years range 44–85 years	Metastatic cancer, local recurrence	Palliative care setting in three palliative care units
Tsai <i>et al.</i> (2007)	Not reported	Female 9 male 15	Mean and range not reported	Advanced cancer	Inpatients recruited from a palliative care unit in a medical centre
Wyatt <i>et al.</i> (2012)	Breast cancer	Female 385 (100%)	Therapy group I mean 55.3 years Therapy group II 54.8 years Control group 57.3 years	Stage III or IV breast cancer, metastasis or recurrence	Outpatients Intervention was conducted

Table 4 (Continued).

Author	Cancer sites	Gender	Age	Cancer stage	Other socio-demographic information
Yamamoto and Nagata (2011)	Gastric cancer, colon cancer, liver cancer, pancreatic carcinoma, breast cancer, uterine cancer, bronchogenic cancer, chronic myelogenous leukaemia	6 female 12 male <i>n</i> = 18	50–59 years, 5 60–69 years, 8 >70 years, 5	Incurable cancer	primarily at women's homes Hospitalized patients

control group received nurse-led supportive care. Acupuncture was performed by a radiation oncologist and a certified medical acupuncturist.

Reflexology (Wyatt *et al.* 2012) was used in a longitudinal randomized trial. The control group received lay foot manipulation (LFM). Reflexology and LFM pressure intervention were delivered in four weekly 30 minute sessions. The reflexology was performed by certified reflexologists, and the LFM providers were lay women who had no training in reflexology but were trained in the LFM protocol. The wrapped warm footbath (Yamamoto & Nagata 2011) intervention involved the lower legs and feet being rubbed with olive oil. The patient's feet were then soaked for 20 minutes in warm water, then washed and wiped dry.

Cognitive behavioural strategies included relaxation, distraction and imagery exercises. Tsai *et al.* (2007) explored the effects of electromyography biofeedback-assisted relaxation. The experimental group received six EMG biofeedback sessions over 4 weeks. Kwekkeboom *et al.* (2010) used 12 cognitive behavioural strategies (e.g. relaxation, distraction and imagery exercises, nature sound recordings) in a one group, examined by means of a pre- and posttest design. The participants received training to use an MP3 player loaded with cognitive behavioural interventions, which they used as needed over 2 weeks.

Outcome measures

A variety of measurement instruments were used to assess pain across the studies. To measure the pain interference and pain intensity, two of the studies used the Brief Pain Inventory (BPI) (Tsai *et al.* 2007, Kwekkeboom *et al.* 2010). In two of the studies, Memorial Pain Assessment Card and BPI were used (Kutner *et al.* 2008, Lopez-Sendin *et al.* 2012). Wyatt *et al.* (2012) used the BPI short form to measure outcomes. Other measurement instruments used for measuring pain were as follows: the Visual Analogue Scale (VAS) and Edmonton Symptom Assessment System (ESAS) (Soden *et al.* 2004, Lim *et al.* 2011, Yamamoto & Nagata 2011). Bennett *et al.* (2010) used the Numerical Rating Scale (NRS) and Short-form McGill Pain Questionnaire (SF-MPQ) as a measurement tool. Jane *et al.* (2009, 2011) used Present Pain Intensity (PPI) with a vertical form of the visual analogy scale (PPI-VAS).

Effects and safety of non-pharmacological interventions for managing cancer pain

Mixed results were reported for the effectiveness of massage in reducing cancer pain in patients with advanced cancer. In one RCT study, there was clinically significant evidence

that massage had, within groups, immediate beneficial effects on pain (95% CI -2.07 to 1.67); although the massage therapy was statistically superior to the control group (mean pain difference between study groups, -0.90 point, $P < 0.001$), it did not attain clinical significance (Kutner *et al.* 2008). In a quasi-experimental trial, Jane *et al.* (2009) examined the time effect of massage therapy and found that it was effective immediately (mean 3.1 , SD 1.4 , $P < 0.001$), as well as over short-term (20–30 min) (mean 2.6 , SD 1.8 , $P < 0.001$), intermediate (1–2.5 hours) (mean 3.0 , SD 1.8 , $P < 0.001$) and long-term (16–18 hours) (mean 3.8 , SD 2.0 , $P < 0.001$) periods. In a later RCT study, Jane *et al.* (2011) also reported that massage reduced pain statistically significantly between groups over time ($P < 0.001$) in a 5-day intervention that included three massage sessions. In one RCT, massage combined with exercises was also reported to reduce pain: between groups, massage was statistically significant in the first evaluation, for BPI worst pain (95% CI -3.8 to -0.08 , $P = 0.036$), BPI pain right now (95% CI -3.9 to -0.1 , $P = 0.027$) and for the first and second evaluation, BPI index (95% CI -4.17 to -1.18 , $P < 0.001$) (Lopez-Sendin 2012). However, Kutner *et al.* (2008) did not find evidence of sustained effects (BPI mean pain, 0.07 points (CI, -0.23 to 0.37 points); BPI worst pain, -0.14 points (CI, -0.59 to 0.31 points) P value not given) of massage therapy in reducing cancer pain. Soden *et al.* (2004) looked for evidence of long-term effects of massage on cancer pain in a RCT, but did not find significant long-term effects in the intervention group compared with the control group. In two of the massage trials (Kutner *et al.* 2008, Jane *et al.* 2009), no adverse events related to the treatment were presented. The other studies did not describe the safety of the intervention.

TENS was shown to have the potential to decrease pain during movement (difference between groups 14.2 , 95% CI $= -3.34$ to 31.76) more than pain during rest (difference between groups -1.32 , 95% CI $= -3.42$ to 0.79). It was well tolerated (Bennett *et al.* 2010). Acupuncture was shown to reduce pain immediately (mean change in ESAS score 1.0 – 2.0 , CI or P value not given) after the intervention, but the benefit was transient and not significant compared with the social attention group. Acupuncture was well tolerated with some minor side effects, but there were no significant or unexpected side effects. (Lim *et al.* 2011). The wrapped warm footbath intervention study reported that participants experienced significant pain relief after the treatment. Compared with the pre-test value, the average VAS score decreased significantly in the experimental group ($P = 0.047$), but significant differences between intervention and control groups were not demonstrated. (Yamamoto &

Nagata 2011). Reflexology did not result in any cancer pain reduction (Wyatt *et al.* 2012).

The effect of EMG biofeedback-assisted relaxation on cancer-related pain was examined in a randomized trial (Tsai *et al.* 2007), which showed that the posttest pain intensity was significantly lower for the experimental group compared with the control group (95% CI $= -2.96$ to -0.21 , $P = 0.011$). Kwekkeboom *et al.* (2010) tested the effect of patient-controlled cognitive behavioural strategies (e.g. relaxation, distraction and imagery exercises and nature sound recordings) on cancer pain in a quasi-experimental trial. The single pre- and posttest group reported that the strategies reduced pain significantly immediately after their application; mean pain scores decreased from 4.54 (SD $= 2.27$) pre-treatment to 2.77 (SD $= 2.06$) posttreatment ($P < 0.01$). The scores 2 weeks after, however, did not differ significantly from the baseline. Adverse events were not evaluated in these studies.

Discussion

The review presents an overview of the effects and safety of non-pharmacological therapies on treating cancer pain among patients with advanced cancer. Although a comprehensive search was undertaken, just 11 studies met the inclusion criteria. There were some methodological limitations in the included studies: the intervention times were short, many from 3 days–2 weeks, only four studies lasted for 4 weeks. (Soden *et al.* 2004, Tsai *et al.* 2007, Lim *et al.* 2011, Wyatt *et al.* 2012). Overall, the sample sizes were small ($n = 9$ – 72) and just two studies had more than 300 ($n = 380$ – 385) participants (Kutner *et al.* 2008, Wyatt *et al.* 2012). In some studies, there was a lack of a usual care control group. Adverse events were not systematically recorded during the intervention in six of the studies.

The non-pharmacological interventions were mostly implemented in inpatient settings. Approximately 49–100% of end-of-life patients want to receive palliative care and be given the opportunity to die at home (Higginson & Sen-Gupta 2000, Beccaro *et al.* 2006). Beccaro *et al.* (2006), however, found that only 68% of patients who wished to die at home had their wish fulfilled. In Finland, only half of patients who wished to die at home were able to do so (Tasmuth *et al.* 2006). Non-pharmacological interventions could be implemented in the home to achieve the best possible management of cancer pain.

Most of the non-pharmacological interventions examined focused on the physical modalities, only two of the studies focused on cognitive modalities (Tsai *et al.* 2007, Kwekkeboom *et al.* 2010). From the physical modalities, massage was the intervention explored most frequently; the

results of the studies were mixed. There was some evidence in all four studies that massage might reduce pain immediately after the intervention, but no sustained effects were reported. A large retrospective ($n = 1290$) study, which included patients with cancer of all cancer stages also showed that massage has a positive effect on managing cancer pain (Cassileth & Vickers 2004). The limitations of the studies and the small number of trials make it impossible to draw conclusions about the safety and positive effects in reducing cancer pain of massage. The same conclusion was reached in a systematic review of massage therapy's effect on cancer symptoms in patients in all stages of cancer (Wilkinson *et al.* 2008a). Even though there is no strong evidence of any effect of massage on cancer symptom management, there have been two qualitative studies on patients with cancer's experiences of massage with respect to the relief of suffering. The patients felt that massage helped to distract them from the frightening experience; it helped to turn negative feelings into positive ones; it was relaxing; it confirmed that patients were being cared and finally, they just felt good. Massage can, indeed, bring about valuable relief from suffering because it just 'feels good'. (Billhult & Dahlgren 2001, Billhult *et al.* 2007).

TENS therapy was found to have the potential to relieve cancer pain, more during pain with movement than when at rest. There were, however, some adverse events in the intervention group. Three of the events were possibly related to the TENS therapy. With just one limited study, it is not possible to draw conclusions about the safety and potential of TENS to reduce pain. Hurlow *et al.* (2012) have undertaken a Cochrane review of the effect of TENS in pain reduction in adult patients with cancer; they were unable to draw any firm conclusions, however, due to a lack of suitable RCTs. The same has to be concluded for acupuncture: in this review, we managed to find only one study that considered acupuncture use in the treatment of pain in patients with advanced cancer, although the results showed that acupuncture may be useful. In addition, Paley *et al.* (2011) showed that there is not enough evidence to draw conclusions about the benefits of acupuncture in pain reduction, based on a Cochrane review including patients with cancer in all cancer stages.

The cognitive modalities were also linked to a reduction in cancer pain. Of the recommended non-pharmacological treatments, only a few of them were represented in the studies examined. We did not manage to find studies considering music, spiritual care, hypnosis, active coping training, cold or ultrasonic stimulation. One reason for this may be that such complementary therapies are less likely to be published in refereed, indexed journals than interventions associated with conventional care (Pan *et al.* 2000).

Bradt and Dileo (2010) undertook a Cochrane systematic review of music therapy and quality of life of people at the end-of-life. A limited number of studies suggested that music therapy may enhance quality of life. Their review was, however, not restricted to patients with cancer. Patients with advanced cancer often suffer spiritual, existential or psychological distress and this can contribute adversely to the patient's physical symptoms in the form of pain (Delgado-Guay *et al.* 2011, Porter & Keefe 2011). Candy *et al.* (2012) found that studies of spiritual care are underestimated and that more research in this field is required. In addition, active coping training and the use of music should be studied. Pain is a phenomenon in which patients' expectations and fears affect the sensation. RCTs may not always get the full view of the phenomenon (Wall 2000). Therefore, qualitative research could give us more information about patients' perceptions of non-pharmacological interventions.

Strengths and limitations of this review

This study was conducted in the form of a systematic review. A search strategy was created with the help of an information specialist. Meticulous searches of four electronic databases were undertaken. To reduce subjective selection bias, the inclusion process and the quality of the articles were carefully assessed by two independent researchers. However, there are some limitations to this study. First, the searches were limited to the period 2000–early 2013. Second, there is a risk of language bias because papers that were not in English, Swedish or Finnish were excluded. Third, there is a possibility that only positive research was identified because of publication bias. For these reasons, some studies may have been missed.

Conclusion

Based on the results of the studies included, it is not possible to draw conclusions about the effects and safety of non-pharmacological interventions with respect to pain reduction among patients with advanced cancer. Massage, attention, relaxation TENS and acupuncture showed promising short-term effects, but there is a need for more rigorous trials with larger samples, longer intervention times and 'usual care' control group, to examine the effects and safety of these interventions. This review focused on patients with advanced cancer; they have a life-threatening illness and short life expectancy. The RCTs and quasi-experimental studies show that such patients are also willing to participate in this type of study.

Treating pain is an international prime goal in palliative care; this review shows that there are several research gaps in the field of non-pharmacological therapies: no studies were found about music, spiritual care, hypnosis, active coping training, cold or ultrasonic stimulation. There is also a lack of studies of non-pharmacological interventions implemented in outpatient settings. Qualitative studies should be undertaken to collect information about patients' perceptions and experiences of non-pharmacological interventions. This review has the potential to increase nurses' and researchers' awareness of the present state of knowledge about the evidence relating to the efficacy and safety of non-pharmacological interventions in managing pain in patients with advanced cancer. However, before using these interventions in practice, more research evidence is needed.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Conflict of interest

No conflict of interest has been declared by the authors.

Author contributions

MH and TP were responsible for the study conception and design. MH and TP performed the data collection. MH and PK were responsible for the quality assessment of the selected studies. MH performed the data synthesis. MH, TP and PK were responsible for drafting the manuscript. TP and PK made critical revisions to the paper for important intellectual content. TP supervised the study.

All authors have agreed on the final version and meet at least one of the following criteria [recommended by the IC-MJE (http://www.icmje.org/ethical_1author.html)]:

- substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data;
- drafting the article or revising it critically for important intellectual content.

Supporting Information Online

Additional Supporting Information may be found in the online version of this article:

Table S1. The excluded articles.

Table S2. Quality appraisal.

References

- Bardia A., Barton D.L., Prokop L.J., Bauer B.A. & Moynihan T.J. (2006) Efficacy of complementary and alternative medicine therapies in relieving cancer pain: a systematic review. *Journal of Clinical Oncology* **24**(34), 5457–5464.
- Beccaro M., Constantini M., Giorgi Rossi P., Miccinesi G., Grimaldi M. & Bruzzi P. (2006) Actual and preferred place of death of cancer patients. Results from the Italian survey of the dying of cancer. *Journal of Epidemiology Community Health* **60**, 412–416.
- Bennett M.I., Johnson M.I., Brown S.R., Radford H., Brown J.M. & Searle R.D. (2010) Feasibility study of Transcutaneous Electrical Nerve Stimulation (TENS) for cancer bone pain. *The Journal of Pain* **11**(4), 351–359.
- van den Beuken-van Everdingen M.H.J., de Rijke J.M., Kessels A.G., Schouten H.C., Kleef M. & Patijn J. (2007a) High prevalence of pain in patients with cancer in a large population-based study in The Netherlands. *Pain* **132**, 312–320.
- van den Beuken-van Everdingen M.H.J., de Rijke J.M., Kessels A.G., Schouten H.C., Kleef M. & Patijn J. (2007b) Prevalence of pain in patients with cancer: a systematic review of the past 40 years. *Annals of Oncology* **18**, 1437–1449.
- Billhult A. & Dahlgren K. (2001) A meaningful relief from suffering. Experiences of massage in cancer care. *Cancer Nursing* **24**(3), 180–184.
- Billhult A., Stener-Victorin E. & Bergbom I. (2007) The experience of massage during chemotherapy treatment in breast cancer patients. *Clinical Nursing Research* **16**(2), 85–99.
- Bradt J. & Dileo C. (2010) Music therapy for end-of-life care. *Cochrane Database of Systematic Reviews* **1**: CD007169. DOI: 10.1002/14651858.CD007169.pub2
- Breivik H., Cherny N., Collett B., de Conno F., Filbet M., Foubert A.J., Cohen R. & Dow L. (2009) Cancer-related pain: a pan-European survey of prevalence, treatment and patient attitudes. *Annals of Oncology* **20**, 1420–1433.
- Candy B., Jones L., Varagunam M., Speck P., Tookman A. & King M. (2012) Spiritual and religious interventions for well-being of adults in the terminal phase of disease. *Cochrane Database of Systematic Reviews* **5**: CD007544. DOI: 10.1002/14651858.CD007544.pub2.
- Cassileth B.R. & Vickers A.J. (2004) Massage therapy for symptom control: outcome study at a major cancer center. *Journal of Pain and Symptom Management* **28**(3), 244–249.
- Centre for Reviews and Dissemination (2008) *Systematic Reviews. CRD's Guidance for Undertaking Reviews in Health Care*. University of York, York.
- Cohen M.M. (2004) CAM practitioners and 'regular' doctors: is integration possible? *Medical Journal* **180**, 645–646.
- Delgado-Guay M.O., Hui D., Parsons H.A., Govan K., De la Cruz M., Thorney S. & Bruera E. (2011) Spirituality, religiosity and spiritual pain in advanced cancer patients. *Journal of Pain and Symptom Management* **41**(6), 986–994.
- Deng G. & Cassileth B.R. (2005) Integrative oncology: complementary therapies for pain, anxiety and mood disturbance. *Complementary & Alternative methods* **55**(2), 109–116.

- Goudas L.C., Bloch R., Gialeli-Goudas M., Lau J. & Carr D.B. (2005) The epidemiology of cancer pain. *Cancer Investigation* 23, 182–190.
- Hansson P. & Lundeberg T. (1999) Transcutaneous electrical nerve stimulation, vibration and acupuncture as pain-relieving measures. In *Textbook of Pain*, 4th edn (Wall P. & Melzack R., eds), Harcourt Publishers Limited, London, pp. 1341–1351.
- Higgins J.P.T. & Green S. (2009) *Cochrane Handbook for Systematic Reviews of Interventions* 5.1.0 [updated March 2011]. The Cochrane Collaboration. Retrieved from <http://www.cochrane-handbook.org> on 1 January 2014.
- Higginson I.J. & Sen-Gupta G.J.A. (2000) Place of care in advanced cancer: a qualitative systematic literature review of patient preferences. *Journal of Palliative Medicine* 3(3), 287–300.
- Hurlow A., Bennett M.I., Robb K.A., Johnson M.I., Simpson K.H. & Oxberry S.G. (2012) Transcutaneous electric nerve stimulation (TENS) for cancer pain in adults. *Cochrane Database of Systematic Reviews* 3, CD006276. DOI: 10.1002/14651858.CD006276.pub3
- Jane S.-W., Wilkie D.J., Gallucci B.B., Beaton R.D. & Huang H.-Y. (2009) Effects of a full-body massage on pain intensity, anxiety and physiological relaxation in taiwanese patients with metastatic bone pain: a pilot study. *Journal of Pain and Symptom Management* 37(4), 754–763.
- Jane S.-W., Chen S.-L., Wilkie D.J., Lin Y.-C., Foreman S.W., Beaton R.D., Fan J.-Y., Lu M.-Y., Wang Y.-Y., Lin Y.-H. & Liao M.-N. (2011) Effects of massage on pain, mood status, relaxation and sleep in Taiwanese patients with metastatic bone pain: a randomized clinical trial. *Pain* 152, 2432–2442.
- Joanna Briggs Institute (2008) Joanna Briggs Institute Reviewers' manual 2008 edition. Retrieved from http://www.joannabriggs.edu.au/Documents/JBIRReviewManual_CiP11449.pdf.
- Jones T. & Evans D. (2000) Conducting a systematic review. *Australian Critical care* 13(2), 66–71.
- Kutner J.S., Smith M.S., Corbin L., Hemphill L., Benton K., Mellis B.K., Beatty B., Felton S., Yamashita T.E., Bryant L.L. & Fairclough D.L. (2008) Massage therapy versus simple touch to improve pain and mood in patients with advanced cancer. *Annals of Internal Medicine* 149, 369–379.
- Kwekkeboom K.L., Abbott-Anderson K. & Wanta B. (2010) Feasibility of a patient-controlled cognitive-behavioral intervention for pain, fatigue and sleep disturbance in cancer. *Oncology Nursing Forum* 37(3), E151–E159.
- Laird B., Colvin L. & Fallon M. (2008) Management of cancer pain: basic principles and neuropathic cancer pain. *European journal of cancer* 44, 1078–1082.
- Lehmann J.F. & de Lateur B.J. (1999) Ultrasound, shortwave, microwave, laser, superficial heat and cold in treatment of pain. In *Textbook of Pain*, 4th edn (Wall P. & Melzack R., eds), Harcourt Publishers Limited, London, pp. 1383–1397.
- Lim J.T.W., Wong E.T. & Aung S.K.H. (2011) Is there a role for acupuncture in the symptom management of patients receiving palliative care for cancer? A pilot study of 20 patients comparing acupuncture with nurse-led supportive care. *Acupuncture Medicine* 29, 173–179.
- Lloyd Jones M. (2004) Application of systematic review methods to qualitative research: practical issues. *Journal of Advanced Nursing* 48(3), 271–278.
- Lopez-Sendin N., Auburquerque-Sendin F., Cleland J.A. & Fernandez-de-las-Penas C. (2012) Effects of physical therapy on pain and mood in patients with terminal cancer: a pilot randomized clinical trial. *The Journal of Alternative and Complementary Medicine* 18(5), 480–486.
- Melzack R. & Wall P. (1965) Pain mechanisms: a new theory. *Science* 150(3699), 971–979.
- Moher D., Liberati A., Tetzlaff J., Altman D.G. & Prisma Group (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *British Medical Journal* 339, 332–339.
- Otis-Green S., Sherman R., Perez M. & Baird R.P. (2002) An integrated Psychosocial-spiritual model for cancer pain management. *Cancer Practice* 10(Suppl 1), S58–S65.
- Paice J.A. & Ferrell B. (2011) The management of cancer pain. *A Cancer Journal for Clinicians* 61(3), 157–182.
- Paley C.A., Johnson M.I., Tashani O.A. & Bagnall A.-M. (2011) Acupuncture for cancer-related pain in adults. *Cochrane Database of Systematic Reviews* 1, CD007753. DOI: 10.1002/14651858.CD007753.pub2
- Pan C.X., Morrison R.S., Ness J., Fugh-Berman A. & Leipzig R.M. (2000) Complementary and alternative medicine in the management of pain, dyspnea and nausea and vomiting near the end of life: a systematic review. *Journal of Pain and Symptom Management* 20(5), 374–387.
- Polit D.F. & Beck C.T. (2011) *Nursing Research. Generating and Assessing Evidence for Nursing Practice*, 9th edn. Lippincott Williams & Wilkins, Philadelphia, PA.
- Porter L.S. & Keefe F.J. (2011) Psychosocial issues in cancer pain. *Current Pain Headache Report* 15, 263–270.
- Soden K., Vincent K. & Craske S. (2004) A randomized controlled trial of aromatherapy massage in a hospice setting. *Palliative medicine* 18, 87–92.
- Sutton L.M., Porter L. & Keefe F.J. (2002) Cancer pain at the end of life: a biopsychosocial perspective. *Pain* 99, 5–10.
- Swarm R., Abernethy A., Angheluescu D., Benedetti C., Bliderman C., Boston B., Cleeland C., Coyle N., deLeon-Casasola O., Eilers J., Ferrell B., Janjan N., Karver S., Levy M., Lynch M., Moryl N., Murphy B., Nesbit S., Oakes L., Obbens E., Paice J., Rabow M., Syrjala K., Urba S. & Weinstein S. (2010) Adult cancer pain. *Journal of the National Comprehensive Cancer Network* 8 (9), 1046–1086.
- Tasmuth T., Saarto T. & Kalso E. (2006) How palliative care of cancer patients is organized between a University Hospital and primary care in Finland. *Acta Oncologica* 45, 325–331.
- The International Association of the Study of Pain (2012) IASP Taxonomy. Pain terms. Retrieved from http://www.iasp-pain.org/AM/Template.cfm?Section=Pain_Definitions on 22 May 2012.
- Tsai P.-S., Chen P.-L., Lai Y.-L., Lee M.-B. & Lin C.-C. (2007) Effects of electromyography biofeedback-assisted relaxation on pain in patients with advanced cancer in a palliative care unit. *Cancer Nursing* 30(5), 347–353.
- Turk D.C. & Okifuji A. (1999) A cognitive-behavioral approach to pain management. In *Textbook of Pain*, 4th edn (Wall P. & Melzack R., eds), Harcourt Publishers Limited, London, pp. 1431–1443.
- Urch C.E. & Dickenson A.H. (2008) Neuropathic pain in cancer. *European Journal of Cancer* 44, 1091–1096.

- Wall P. (2000) *Pain-The Science of Suffering*. Columbia University Press, New York.
- Whiting L.S. (2009) Systematic review protocols. *Nurse Researcher* 17(1), 34–43.
- Whittemore R. (2005) Combining evidence in nursing practice. *Nursing Research* 54(5), 56–62.
- Wilkinson S., Barnes K. & Storey L. (2008a) Massage for symptom relief in patients with cancer: a systematic review. *Journal of Advanced Nursing* 63(5), 430–439.
- Wilkinson S., Lockhart K., Gambles M. & Storey L. (2008b) Reflexology for symptom relief in patients with cancer. *Cancer Nursing* 31, 354–360.
- World Health Organization (2005) Knowledge into Action. Cancer Control. WHO Guide for Effective Programmes. Retrieved from http://whqlibdoc.who.int/publications/2006/9241546999_eng.pdf on 10 January 2013.
- World Health Organization (2013) WHO Definition of Palliative Care. <http://www.who.int/cancer/palliative/definition/en/> on 15 January 2013.
- Wyatt G., Sikorskii A., Rahbar M.H., Victorson D. & You M. (2012) Health-related quality-of-life outcomes: a reflexology trial with patients with advanced-stage breast cancer. *Oncology Nursing Forum* 39(6), 568–577.
- Yamamoto K. & Nagata S. (2011) Physiological and psychological evaluation of the wrapped warm footbath as a complementary nursing therapy to induce relaxation in hospitalized patients with incurable cancer. *Cancer Nursing* 34(3), 185–192.

The *Journal of Advanced Nursing (JAN)* is an international, peer-reviewed, scientific journal. *JAN* contributes to the advancement of evidence-based nursing, midwifery and health care by disseminating high quality research and scholarship of contemporary relevance and with potential to advance knowledge for practice, education, management or policy. *JAN* publishes research reviews, original research reports and methodological and theoretical papers.

For further information, please visit *JAN* on the Wiley Online Library website: www.wileyonlinelibrary.com/journal/jan

Reasons to publish your work in *JAN*:

- **High-impact forum:** the world's most cited nursing journal, with an Impact Factor of 1.527 – ranked 14/101 in the 2012 ISI Journal Citation Reports © (Nursing (Social Science)).
- **Most read nursing journal in the world:** over 3 million articles downloaded online per year and accessible in over 10,000 libraries worldwide (including over 3,500 in developing countries with free or low cost access).
- **Fast and easy online submission:** online submission at <http://mc.manuscriptcentral.com/jan>.
- **Positive publishing experience:** rapid double-blind peer review with constructive feedback.
- **Rapid online publication in five weeks:** average time from final manuscript arriving in production to online publication.
- **Online Open:** the option to pay to make your article freely and openly accessible to non-subscribers upon publication on Wiley Online Library, as well as the option to deposit the article in your own or your funding agency's preferred archive (e.g. PubMed).